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Neurobehavioural effects of developmental toxicity

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Summary

Neurodevelopmental disabilities, including autism, attention-deficit hyperactivity disorder, dyslexia, and other cognitive impairments, affect millions of children worldwide, and some diagnoses seem to be increasing in frequency.

Industrial chemicals that injure the developing brain are among the known causes for this rise in prevalence.

In 2006, we did a systematic review and identified five industrial chemicals as developmental neurotoxicants: lead, methylmercury, polychlorinated biphenyls, arsenic, and toluene.

Since 2006, epidemiological studies have documented six additional developmental neurotoxicants — manganese, fluoride, chlorpyrifos, dichlorodiphenyltrichloroethane, tetrachloroethylene, and the polybrominated diphenyl ethers.

We postulate that even more neurotoxicants remain undiscovered.

To control the pandemic of developmental neurotoxicity, we propose a global prevention strategy.

Untested chemicals should not be presumed to be safe to brain development, and chemicals in existing use and all new chemicals must therefore be tested for developmental neurotoxicity.

To coordinate these efforts and to accelerate translation of science into prevention, we propose the urgent formation of a new international clearinghouse.

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[selections]

Exposure to air pollution can cause neurodevelopmental delays and disorders of behavioural functions.[68](#), [69](#) Of the individual components of air pollution, carbon monoxide is a well-documented neurotoxicant, and indoor exposure to this substance has now been linked to deficient neurobehavioural performance in children.[70](#) Less clear is the reported contribution of nitrogen oxides to neurodevelopmental deficits,[71](#) since these compounds often co-occur with carbon monoxide as part of complex emissions. Tobacco smoke is a complex mixture of hundreds of chemical compounds and is now a well-documented cause of developmental neurotoxicity.[72](#) Infants exposed prenatally to polycyclic aromatic hydrocarbons from traffic exhausts at 5 years of age showed greater cognitive impairment and lower IQ than those exposed to lower levels of these compounds.[68](#)

Developmental neurotoxicity and clinical neurology

Exposures in early life to developmental neurotoxicants are now being linked to specific clinical syndromes in children. For example, an increased risk of attention-deficit hyperactivity disorder has been linked to prenatal exposures to manganese, organophosphates,[75](#) and phthalates.[76](#) Phthalates have also been linked to behaviours that resemble components of autism spectrum disorder.[77](#) Prenatal exposure to automotive air pollution in California, USA, has been linked to an increased risk for autism spectrum disorder.[78](#)

The persistent decrements in intelligence documented in children, adolescents, and young adults exposed in early life to neurotoxicants could presage the development of neurodegenerative disease later in life. Thus, accumulated exposure to lead is associated with cognitive decline in the elderly.[79](#) Manganese exposure may lead to parkinsonism, and experimental studies have reported Parkinson's disease as a result of developmental exposures to the insecticide rotenone, the herbicides paraquat and maneb, and the solvent trichloroethylene.[80](#) Any environmental exposure that increases the risk of neurodegenerative disorders in later life ([figure 1](#)) requires urgent investigation as the world's population continues to age.[81](#)

The expanding complement of neurotoxicants

In our 2006 review,[6](#) we expressed concern that additional developmental neurotoxicants might lie

undiscovered in the 201 chemicals that were then known to be neurotoxic to human adults, in the roughly 1000 chemicals known to be neurotoxic in animal species, and in the many thousands of industrial chemicals and pesticides that have never been tested for neurotoxicity. Exposure to neurotoxic chemicals is not rare, since almost half of the 201 known human neurotoxicants are regarded as high production volume chemicals.

Our updated literature review shows that since 2006 the list of recognised human neurotoxicants has expanded by 12 chemicals, from 202 (including ethanol) to 214 ([table 1](#) and [appendix](#))—that is, by about two substances per year. Many of these chemicals are widely used and disseminated extensively in the global environment. Of the newly identified neurodevelopmental toxicants, pesticides constitute the largest group, as was already the case in 2006. In the same 7-year period, the number of known developmental neurotoxicants has doubled from six to 12 ([table 2](#)). Although the pace of scientific discovery of new neurodevelopmental hazards is more rapid today than in the past, it is still slower than the identification of adult neurotoxicants.

The gap that exists between the number of substances known to be toxic to the adult brain and the smaller number known to be toxic to the much more vulnerable developing brain is unlikely to close in the near future. This discrepancy is attributable to the fact that toxicity to the adult brain is usually discovered as a result of acute poisoning incidents, typically with a clear and immediate association between causative exposure and adverse effects, as occurs for workplace exposures or suicide attempts. By contrast, the recognition of developmental neurotoxicity relies on two sets of evidence collected at two different points in time: exposure data (often obtained from the mother during pregnancy), and data for the child's postnatal neurobehavioural development (often obtained 5–10 years later). Because brain functions develop sequentially, the full effects of early neurotoxic damage might not become apparent until school age or beyond. The most reliable evidence of developmental neurotoxicity is obtained through prospective studies that include real-time recording of information about exposure in early life followed by serial clinical assessments of the child. Such research is inherently slow and is hampered by the difficulty of reliable assessment of exposures to individual toxicants in complex mixtures.

Consequences of developmental neurotoxicity

Developmental neurotoxicity causes brain damage that is too often untreatable and frequently permanent. The consequence of such brain damage is impaired CNS function that lasts a lifetime and might result in reduced intelligence, as expressed in terms of lost IQ points, or disruption in behaviour. A recent study compared the estimated total IQ losses from major paediatric causes and showed that the magnitude of losses attributable to lead, pesticides, and other neurotoxicants was in the same range as, or even greater than, the losses associated with medical events such as preterm birth, traumatic brain injury, brain tumours, and congenital heart disease ([table 3](#)).⁹⁴

Loss of cognitive skills reduces children's academic and economic attainments and has substantial long-term economic effects on societies.⁴ Thus, each loss of one IQ point has been estimated to decrease average lifetime earnings capacity by about €12 000 or US\$18 000 in 2008 currencies.⁹⁶ The most recent estimates from the USA indicate that the annual costs of childhood lead poisoning are about

US\$50 billion and that the annual costs of methylmercury toxicity are roughly US\$5 billion.⁹⁷ In the European Union, methylmercury exposure is estimated to cause a loss of about 600 000 IQ points every year, corresponding to an annual economic loss of close to €10 billion. In France alone, lead exposure is associated with IQ losses that correspond to annual costs that might exceed €20 billion.⁹⁸ Since IQ losses represent only one aspect of developmental neurotoxicity, the total costs are surely even higher.

Evidence from worldwide sources indicates that average national IQ scores are associated with gross domestic product (GDP)—a correlation that might be causal in both directions.⁹⁹ Thus, poverty can cause low IQ, but the opposite is also true. In view of the widespread exposures to lead, pesticides, and other neurotoxicants in developing countries, where chemical controls might be ineffective compared with those in more developed countries,^{100, 101} developmental exposures to industrial chemicals could contribute substantially to the recorded correlation between IQ and GDP. If this theory is true, developing countries could take decades to emerge from poverty. Consequently, pollution abatement might then be delayed, and a vicious circle can result.

The antisocial behaviour, criminal behaviour, violence, and substance abuse that seem to result from early-life exposures to some neurotoxic chemicals result in increased needs for special educational services, institutionalisation, and even incarceration. In the USA, the murder rate fell sharply 20 years after the removal of lead from petrol,¹⁰² a finding consistent with the idea that exposure to lead in early life is a powerful determinant of behaviour decades later. Although poorly quantified, such behavioural and social consequences of neurodevelopmental toxicity are potentially very costly.⁷⁶

Prevention of developmental neurotoxicity caused by industrial chemicals is highly cost effective. A study that quantified the gains resulting from the phase-out of lead additives from petrol reported that in the USA alone, the introduction of lead-free petrol has generated an economic benefit of \$200 billion in each annual birth cohort since 1980,¹⁰³ an aggregate benefit in the past 30 years of over \$3 trillion. This success has since been repeated in more than 150 countries, resulting in vast additional savings. Every US\$1 spent to reduce lead hazards is estimated to produce a benefit of US\$17–220, which represents a cost-benefit ratio that is even better than that for vaccines.⁴ Furthermore, the costs associated with the late-life consequences of developmental neurotoxicity are enormous, and the benefits from prevention of degenerative brain disorders could be very substantial.

New methods to identify developmental neurotoxicants

New toxicological methods now allow a rational strategy for the identification of developmental neurotoxicants based on a multidisciplinary approach.¹⁰⁴ A new guideline has been approved as a standardised approach for the identification of developmental neurotoxicants.¹⁰⁵ However, completion of such tests is expensive and requires the use of many laboratory animals, and reliance on mammals for chemicals testing purposes needs to be reduced.¹⁰⁶ US governmental agencies have established the National Center for Computational Toxicology and an initiative—the Tox 21 Program—to promote the evolution of toxicology from a mainly observational science to a predominantly predictive science.¹⁰⁷

In-vitro methods have now reached a level of predictive validity that means they can be applied to

neurotoxicity testing.¹⁰⁸ Some of these tests are based on neural stem cells. Although these cell systems do not have a blood–brain barrier and particular metabolising enzymes, these approaches are highly promising. As a further option, data for protein links and protein–protein interactions can now be used to explore potential neurotoxicity in silico,¹⁰⁹ thus showing that existing computational methods might predict potential toxic effects.¹¹⁰

In summary, use of the whole range of approaches along with clinical and epidemiological evidence, when available, should enable the integration of information for use in at least a tentative risk assessment. With these methods, we anticipate that the pace of scientific discovery in developmental neurotoxicology will accelerate further in the years ahead.

Conclusions and recommendations

The updated findings presented in this Review confirm and extend our 2006 conclusions.⁶ During the 7 years since our previous report, the number of industrial chemicals recognised to be developmental neurotoxicants has doubled. Exposures to these industrial chemicals in the environment contribute to the pandemic of developmental neurotoxicity.

Two major obstacles impede efforts to control the global pandemic of developmental neurotoxicity. These barriers, which we noted in our previous review⁶ and were recently underlined by the US National Research Council,¹¹¹ are: large gaps in the testing of chemicals for developmental neurotoxicity, which results in a paucity of systematic data to guide prevention; and the huge amount of proof needed for regulation. Thus, very few chemicals have been regulated as a result of developmental neurotoxicity.

The presumption that new chemicals and technologies are safe until proven otherwise is a fundamental problem.¹¹¹ Classic examples of new chemicals that were introduced because they conveyed certain benefits, but were later shown to cause great harm, include several neurotoxicants, asbestos, thalidomide, diethylstilboestrol, and the chlorofluorocarbons.¹¹² A recurring theme in each of these cases was that commercial introduction and wide dissemination of the chemicals preceded any systematic effort to assess potential toxicity. Particularly absent were advance efforts to study possible effects on children's health or the potential of exposures in early life to disrupt early development. Similar challenges have been confronted in other public health disasters, such as those caused by tobacco smoking, alcohol use, and refined foods. These problems have been recently termed industrial epidemics.¹¹³

To control the pandemic of developmental neurotoxicity, we propose a coordinated international strategy ([panel](#)). Mandatory and transparent assessment of evidence for neurotoxicity is the foundation of this strategy. Assessment of toxicity must be followed by governmental regulation and market intervention. Voluntary controls seem to be of little value.¹¹

Panel

Recommendations for an international clearinghouse on neurotoxicity

The main purpose of this agency would be to promote optimum brain health, not just avoidance of neurological disease, by inspiring, facilitating, and coordinating research and public policies that aim to protect brain development during the most sensitive life stages. The main efforts would aim to:

- Screen industrial chemicals present in human exposures for neurotoxic effects so that hazardous substances can be identified for tighter control
- Stimulate and coordinate new research to understand how toxic chemicals interfere with brain development and how best to prevent long-term dysfunctions and deficits
- Function as a clearinghouse for research data and strategies by gathering and assessing documentation about brain toxicity and stimulating international collaboration on research and prevention
- Promote policy development aimed at protecting vulnerable populations against chemicals that are toxic to the brain without needing unrealistic amounts of scientific proof

The three pillars of our proposed strategy are: legally mandated testing of existing industrial chemicals and pesticides already in commerce, with prioritisation of those with the most widespread use, and incorporation of new assessment technologies; legally mandated premarket evaluation of new chemicals before they enter markets, with use of precautionary approaches for chemical testing that recognise the unique vulnerability of the developing brain; and the formation of a new clearinghouse for neurotoxicity as a parallel to the International Agency for Research on Cancer. This new agency will assess industrial chemicals for developmental neurotoxicity with a precautionary approach that emphasises prevention and does not require absolute proof of toxicity. It will facilitate and coordinate epidemiological and toxicological studies and will lead the urgently needed global programmes for prevention.

These new approaches must reverse the dangerous presumption that new chemicals and technologies are safe until proven otherwise. They must also overcome the existing requirement to produce absolute proof of toxicity before action can be started to protect children against neurotoxic substances. Precautionary interpretation of data about developmental neurotoxicity should take into account the very large individual and societal costs that result from failure to act on available documentation to prevent disease in children.¹¹⁴ Academic research has often favoured scepticism and required extensive replication before acceptance of a hypothesis,¹¹⁴ thereby adding to the inertia in toxicology and environmental health research and the consequent disregard of many other potential neurotoxicants.¹¹⁵ Additionally, the strength of evidence that is needed to constitute “proof” should be analysed in a societal perspective, so that the implications of ignoring a developmental neurotoxicant and of failing to act on the basis of available data are also taken into account.

Finally, we emphasise that the total number of neurotoxic substances now recognised almost certainly represents an underestimate of the true number of developmental neurotoxicants that have been released into the global environment. Our very great concern is that children worldwide are being exposed to unrecognised toxic chemicals that are silently eroding intelligence, disrupting behaviours, truncating future achievements, and damaging societies, perhaps most seriously in developing countries. A new framework of action is needed.

Search strategy and selection criteria

We identified studies published since 2006 on the neurotoxic effects of industrial chemicals in human beings by using the search terms “neurotoxicity syndromes”[MeSH], “neurotoxic”, “neurologic”, or “neuro*”, combined with “exposure” and “poisoning” in PubMed, from 2006 to the end of 2012. For developmental neurotoxicity, the search terms were “prenatal exposure delayed effects”[MeSH], “maternal exposure” or “maternal fetal exchange”, “developmental disabilities/chemically induced” and “neurotoxins”, all of which were searched for with the limiters “All Child: 0–18 years, Human”. We also used references cited in the publications retrieved.

Contributors

Both authors did the literature review, wrote and revised the report, and approved the final version.

Conflicts of interest

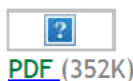
PG has provided paid expert testimony about mercury toxicology for the US Department of Justice. P.J.L. has provided paid expert testimony in cases of childhood lead poisoning. We declare that we have no other conflicts of interest.

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Supplementary Material

Supplementary appendix



References

- 1 Bloom B, Cohen RA, Freeman G. Summary health statistics for U.S. children: National Health

Interview Survey, 2009. *Vital Health Stat* 2010; **10**: 1-82. [PubMed](#)

[2](#) Landrigan PJ, Lambertini L, Birnbaum LS. A research strategy to discover the environmental causes of autism and neurodevelopmental disabilities. *Environ Health Perspect* 2012; **120**: a258-a260. [CrossRef](#) | [PubMed](#)

[3](#) Bellinger DC. Interpreting epidemiologic studies of developmental neurotoxicity: conceptual and analytic issues. *Neurotoxicol Teratol* 2009; **31**: 267-274. [CrossRef](#) | [PubMed](#)

[4](#) Gould E. Childhood lead poisoning: conservative estimates of the social and economic benefits of lead hazard control. *Environ Health Perspect* 2009; **117**: 1162-1167. [PubMed](#)

[5](#) National Research Council. Scientific frontiers in developmental toxicology and risk assessment. Washington, DC: National Academies Press, 2000.

[6](#) Grandjean P, Landrigan PJ. Developmental neurotoxicity of industrial chemicals. *Lancet* 2006; **368**: 2167-2178. [Summary](#) | [Full Text](#) | [PDF\(163KB\)](#) | [CrossRef](#) | [PubMed](#)

[7](#) Grandjean P. Only one chance. How environmental pollution impairs brain development – and how to protect the brains of the next generation. New York: Oxford University Press, 2013.

[8](#) Rice D, Barone S. Critical periods of vulnerability for the developing nervous system: evidence from humans and animal models. *Environ Health Perspect* 2000; **108** (suppl 3): 511-533. [CrossRef](#) | [PubMed](#)

[9](#) Needleman HL. The removal of lead from gasoline: historical and personal reflections. *Environ Res* 2000; **84**: 20-35. [CrossRef](#) | [PubMed](#)

[10](#) Grandjean P, Satoh H, Murata K, Eto K. Adverse effects of methylmercury: environmental health research implications. *Environ Health Perspect* 2010; **118**: 1137-1145. [CrossRef](#) | [PubMed](#)

[11](#) Landrigan PJ, Goldman LR. Children's vulnerability to toxic chemicals: a challenge and opportunity to strengthen health and environmental policy. *Health Aff* 2011; **30**: 842-850. [PubMed](#)

[12](#) Weiss B. Food additives and environmental chemicals as sources of childhood behavior disorders. *J Am Acad Child Psychiatry* 1982; **21**: 144-152. [CrossRef](#) | [PubMed](#)

[13](#) Needham LL, Grandjean P, Heinzow B, et al. Partition of environmental chemicals between maternal and fetal blood and tissues. *Environ Sci Technol* 2011; **45**: 1121-1126. [CrossRef](#) | [PubMed](#)

[14](#) Environmental Working Group. Body burden—the pollution in newborns. Washington, DC: Environmental Working Group, 2005.

[15](#) Zheng W, Aschner M, Gherzi-Egea JF. Brain barrier systems: a new frontier in metal neurotoxicological research. *Toxicol Appl Pharmacol* 2003; **192**: 1-11. [CrossRef](#) | [PubMed](#)

[16](#) Bose R, Onishchenko N, Edoff K, Janson Lang AM, Ceccatelli S. Inherited effects of low-dose exposure to methylmercury in neural stem cells. *Toxicol Sci* 2012; **130**: 383-390. [CrossRef](#) | [PubMed](#)

[17](#) Costa LG. Current issues in organophosphate toxicology. *Clin Chim Acta* 2006; **366**: 1-13. [CrossRef](#) | [PubMed](#)

[18](#) Augusti-Tocco G, Biagioni S, Tata AM. Acetylcholine and regulation of gene expression in developing systems. *J Mol Neurosci* 2006; **30**: 45-48. [CrossRef](#) | [PubMed](#)

- [19](#) Roth TL. Epigenetics of neurobiology and behavior during development and adulthood. *Dev Psychobiol* 2012; **54**: 590-597. [CrossRef](#) | [PubMed](#)
- [20](#) Lanphear BP, Hornung R, Khoury J, et al. Low-level environmental lead exposure and children's intellectual function: an international pooled analysis. *Environ Health Perspect* 2005; **113**: 894-899. [CrossRef](#) | [PubMed](#)
- [21](#) Budtz-Jorgensen E, Bellinger D, Lanphear B, Grandjean P. An international pooled analysis for obtaining a benchmark dose for environmental lead exposure in children. *Risk Anal* 2013; **33**: 450-461. [CrossRef](#) | [PubMed](#)
- [22](#) Grandjean P. Even low-dose lead exposure is hazardous. *Lancet* 2010; **376**: 855-856. [Full Text](#) | [PDF\(433KB\)](#) | [CrossRef](#) | [PubMed](#)
- [23](#) Mazumdar M, Bellinger DC, Gregas M, Abanilla K, Bacic J, Needleman HL. Low-level environmental lead exposure in childhood and adult intellectual function: a follow-up study. *Environ Health* 2011; **10**: 24. [CrossRef](#) | [PubMed](#)
- [24](#) Cecil KM, Brubaker CJ, Adler CM, et al. Decreased brain volume in adults with childhood lead exposure. *PLoS Med* 2008; **5**: e112. [CrossRef](#) | [PubMed](#)
- [25](#) Zhang N, Baker HW, Tufts M, Raymond RE, Salihu H, Elliott MR. Early childhood lead exposure and academic achievement: evidence from Detroit public schools, 2008–2010. *Am J Public Health* 2013; **103**: e72-e77. [CrossRef](#) | [PubMed](#)
- [26](#) Fergusson DM, Boden JM, Horwood LJ. Dentine lead levels in childhood and criminal behaviour in late adolescence and early adulthood. *J Epidemiol Community Health* 2008; **62**: 1045-1050. [PubMed](#)
- [27](#) Wright JP, Dietrich KN, Ris MD, et al. Association of prenatal and childhood blood lead concentrations with criminal arrests in early adulthood. *PLoS Med* 2008; **5**: e101. [CrossRef](#) | [PubMed](#)
- [28](#) Oken E, Bellinger DC. Fish consumption, methylmercury and child neurodevelopment. *Curr Opin Pediatr* 2008; **20**: 178-183. [CrossRef](#) | [PubMed](#)
- [29](#) Debes F, Budtz-Jorgensen E, Weihe P, White RF, Grandjean P. Impact of prenatal methylmercury exposure on neurobehavioral function at age 14 years. *Neurotoxicol Teratol* 2006; **28**: 536-547. [CrossRef](#) | [PubMed](#)
- [30](#) Julvez J, Smith GD, Golding J, et al. Genetic predisposition to cognitive deficit at age 8 years associated with prenatal methylmercury exposure. *Epidemiology* 2013; **24**: 643-650. [CrossRef](#) | [PubMed](#)
- [31](#) White RF, Palumbo CL, Yurgelun-Todd DA, et al. Functional MRI approach to developmental methylmercury and polychlorinated biphenyl neurotoxicity. *Neurotoxicology* 2011; **32**: 975-980. [CrossRef](#) | [PubMed](#)
- [32](#) Budtz-Jorgensen E, Grandjean P, Weihe P. Separation of risks and benefits of seafood intake. *Environ Health Perspect* 2007; **115**: 323-327. [CrossRef](#) | [PubMed](#)
- [33](#) Strain JJ, Davidson PW, Bonham MP, et al. Associations of maternal long-chain polyunsaturated fatty acids, methyl mercury, and infant development in the Seychelles Child Development Nutrition Study. *Neurotoxicology* 2008; **29**: 776-782. [CrossRef](#) | [PubMed](#)
- [34](#) Wasserman GA, Liu X, Parvez F, et al. Water arsenic exposure and intellectual function in 6-year-old

children in Araihaazar, Bangladesh. *Environ Health Perspect* 2007; 115: 285-289. [CrossRef](#) | [PubMed](#)

[35](#) Hamadani JD, Tofail F, Nermell B, et al. Critical windows of exposure for arsenic-associated impairment of cognitive function in pre-school girls and boys: a population-based cohort study. *Int J Epidemiol* 2011; 40: 1593-1604. [PubMed](#)

[36](#) Tanaka H, Tsukuma H, Oshima A. Long-term prospective study of 6104 survivors of arsenic poisoning during infancy due to contaminated milk powder in 1955. *J Epidemiol* 2010; 20: 439-445. [CrossRef](#) | [PubMed](#)

[37](#) Engel SM, Wolff MS. Causal inference considerations for endocrine disruptor research in children's health. *Annu Rev Public Health* 2013; 34: 139-158. [CrossRef](#) | [PubMed](#)

[38](#) Mattson SN, Crocker N, Nguyen TT. Fetal alcohol spectrum disorders: neuropsychological and behavioral features. *Neuropsychol Rev* 2011; 21: 81-101. [PubMed](#)

[39](#) Khan K, Wasserman GA, Liu X, et al. Manganese exposure from drinking water and children's academic achievement. *Neurotoxicology* 2012; 33: 91-97. [CrossRef](#) | [PubMed](#)

[40](#) Bouchard M, Laforest F, Vandelac L, Bellinger D, Mergler D. Hair manganese and hyperactive behaviors: pilot study of school-age children exposed through tap water. *Environ Health Perspect* 2007; 115: 122-127. [CrossRef](#) | [PubMed](#)

[41](#) Riojas-Rodriguez H, Solis-Vivanco R, Schilman A, et al. Intellectual function in Mexican children living in a mining area and environmentally exposed to manganese. *Environ Health Perspect* 2010; 118: 1465-1470. [CrossRef](#) | [PubMed](#)

[42](#) Lucchini RG, Guazzetti S, Zoni S, et al. Tremor, olfactory and motor changes in Italian adolescents exposed to historical ferro-manganese emission. *Neurotoxicology* 2012; 33: 687-696. [CrossRef](#) | [PubMed](#)

[43](#) Moreno JA, Yeomans EC, Streifel KM, Brattin BL, Taylor RJ, Tjalkens RB. Age-dependent susceptibility to manganese-induced neurological dysfunction. *Toxicol Sci* 2009; 112: 394-404. [CrossRef](#) | [PubMed](#)

[44](#) Choi AL, Sun G, Zhang Y, Grandjean P. Developmental fluoride neurotoxicity: a systematic review and meta-analysis. *Environ Health Perspect* 2012; 120: 1362-1368. [CrossRef](#) | [PubMed](#)

[45](#) Julvez J, Grandjean P. Neurodevelopmental toxicity risks due to occupational exposure to industrial chemicals during pregnancy. *Ind Health* 2009; 47: 459-468. [CrossRef](#) | [PubMed](#)

[46](#) Pele F, Muckle G, Costet N, et al. Occupational solvent exposure during pregnancy and child behaviour at age 2. *Occup Environ Med* 2013; 70: 114-119. [CrossRef](#) | [PubMed](#)

[47](#) Janulewicz PA, White RF, Martin BM, et al. Adult neuropsychological performance following prenatal and early postnatal exposure to tetrachloroethylene (PCE)-contaminated drinking water. *Neurotoxicol Teratol* 2012; 34: 350-359. [CrossRef](#) | [PubMed](#)

[48](#) Kofman O, Berger A, Massarwa A, Friedman A, Jaffar AA. Motor inhibition and learning impairments in school-aged children following exposure to organophosphate pesticides in infancy. *Pediatr Res* 2006; 60: 88-92. [CrossRef](#) | [PubMed](#)

[49](#) London L, Beseler C, Bouchard MF, et al. Neurobehavioral and neurodevelopmental effects of

pesticide exposures. *Neurotoxicology* 2012; **33**: 887-896. [CrossRef](#) | [PubMed](#)

[50](#) Torres-Sanchez L, Schnaas L, Rothenberg SJ, et al. Prenatal p,p'-DDE exposure and neurodevelopment among children 3.5–5 years of age. *Environ Health Perspect* 2013; **121**: 263-268. [CrossRef](#) | [PubMed](#)

[51](#) Boucher O, Simard MN, Muckle G, et al. Exposure to an organochlorine pesticide (chlordecone) and development of 18-month-old infants. *Neurotoxicology* 2013; **35**: 162-168. [CrossRef](#) | [PubMed](#)

[52](#) Rauh V, Arunajadai S, Horton M, et al. 7-year neurodevelopmental scores and prenatal exposure to chlorpyrifos, a common agricultural pesticide. *Environ Health Perspect* 2011; **119**: 1196-1201. [CrossRef](#) | [PubMed](#)

[53](#) Bouchard MF, Chevrier J, Harley KG, et al. Prenatal exposure to organophosphate pesticides and IQ in 7-year old children. *Environ Health Perspect* 2011; **119**: 1189-1195. [CrossRef](#) | [PubMed](#)

[54](#) Engel SM, Wetmur J, Chen J, et al. Prenatal exposure to organophosphates, paraoxonase 1, and cognitive development in childhood. *Environ Health Perspect* 2011; **119**: 1182-1188. [CrossRef](#) | [PubMed](#)

[55](#) Rauh VA, Perera FP, Horton MK, et al. Brain anomalies in children exposed prenatally to a common organophosphate pesticide. *Proc Natl Acad Sci USA* 2012; **109**: 7871-7876. [PubMed](#)

[56](#) Bjorling-Poulsen M, Andersen HR, Grandjean P. Potential developmental neurotoxicity of pesticides used in Europe. *Environ Health* 2008; **7**: 50. [CrossRef](#) | [PubMed](#)

[57](#) Ostrea EM, Reyes A, Villanueva-Uy E, et al. Fetal exposure to propoxur and abnormal child neurodevelopment at 2 years of age. *Neurotoxicology* 2012; **33**: 669-675. [CrossRef](#) | [PubMed](#)

[58](#) Horton MK, Rundle A, Camann DE, Boyd Barr D, Rauh VA, Whyatt RM. Impact of prenatal exposure to piperonyl butoxide and permethrin on 36-month neurodevelopment. *Pediatrics* 2011; **127**: e699-e706. [CrossRef](#) | [PubMed](#)

[59](#) Dingemans MM, van den Berg M, Westerink RH. Neurotoxicity of brominated flame retardants: (in)direct effects of parent and hydroxylated polybrominated diphenyl ethers on the (developing) nervous system. *Environ Health Perspect* 2011; **119**: 900-907. [CrossRef](#) | [PubMed](#)

[60](#) Roze E, Meijer L, Bakker A, Van Braeckel KN, Sauer PJ, Bos AF. Prenatal exposure to organohalogens, including brominated flame retardants, influences motor, cognitive, and behavioral performance at school age. *Environ Health Perspect* 2009; **117**: 1953-1958. [CrossRef](#) | [PubMed](#)

[61](#) Herbstman JB, Sjodin A, Kurzon M, et al. Prenatal exposure to PBDEs and neurodevelopment. *Environ Health Perspect* 2010; **118**: 712-719. [CrossRef](#) | [PubMed](#)

[62](#) Eskenazi B, Chevrier J, Rauch SA, et al. In utero and childhood polybrominated diphenyl ether (PBDE) exposures and neurodevelopment in the CHAMACOS study. *Environ Health Perspect* 2013; **121**: 257-262. [CrossRef](#) | [PubMed](#)

[63](#) Grandjean P, Budtz-Jorgensen E. An ignored risk factor in toxicology: the total imprecision of exposure assessment. *Pure Appl Chem* 2010; **82**: 383-391. [CrossRef](#) | [PubMed](#)

[64](#) Vandenberg LN, Colborn T, Hayes TB, et al. Hormones and endocrine-disrupting chemicals: low-dose effects and nonmonotonic dose responses. *Endocr Rev* 2012; **33**: 378-455. [CrossRef](#) | [PubMed](#)

[65](#) Engel SM, Miodovnik A, Canfield RL, et al. Prenatal phthalate exposure is associated with childhood

behavior and executive functioning. *Environ Health Perspect* 2010; **118**: 565-571. [PubMed](#)

[66](#) Swan SH, Liu F, Hines M, et al. Prenatal phthalate exposure and reduced masculine play in boys. *Int J Androl* 2010; **33**:259-269. [CrossRef](#) | [PubMed](#)

[67](#) Braun JM, Kalkbrenner AE, Calafat AM, et al. Impact of early-life bisphenol A exposure on behavior and executive function in children. *Pediatrics* 2011; **128**: 873-882. [CrossRef](#) | [PubMed](#)

[68](#) Perera FP, Li Z, Whyatt R, et al. Prenatal airborne polycyclic aromatic hydrocarbon exposure and child IQ at age 5 years. *Pediatrics* 2009; **124**: e195-e202. [CrossRef](#) | [PubMed](#)

[69](#) Calderon-Garciduenas L, Mora-Tiscareno A, Ontiveros E, et al. Air pollution, cognitive deficits and brain abnormalities: a pilot study with children and dogs. *Brain Cogn* 2008; **68**: 117-127. [PubMed](#)

[70](#) Dix-Cooper L, Eskenazi B, Romero C, Balmes J, Smith KR. Neurodevelopmental performance among school age children in rural Guatemala is associated with prenatal and postnatal exposure to carbon monoxide, a marker for exposure to woodsmoke. *Neurotoxicology* 2012; **33**: 246-254. [CrossRef](#) | [PubMed](#)

[71](#) Vrijheid M, Martinez D, Aguilera I, et al. Indoor air pollution from gas cooking and infant neurodevelopment. *Epidemiology* 2012; **23**: 23-32. [PubMed](#)

[72](#) Hernandez-Martinez C, Arijia Val V, Escribano Subias J, Canals Sans J. A longitudinal study on the effects of maternal smoking and secondhand smoke exposure during pregnancy on neonatal neurobehavior. *Early Hum Dev* 2012; **88**: 403-408. [CrossRef](#) | [PubMed](#)

[73](#) Mariussen E. Neurotoxic effects of perfluoroalkylated compounds: mechanisms of action and environmental relevance. *Arch Toxicol* 2012; **86**: 1349-1367. [CrossRef](#) | [PubMed](#)

[74](#) Gump BB, Wu Q, Dumas AK, Kannan K. Perfluorochemical (PFC) exposure in children: associations with impaired response inhibition. *Environ Sci Technol* 2011; **45**: 8151-8159. [CrossRef](#) | [PubMed](#)

[75](#) Froehlich TE, Anixt JS, Loe IM, Chirdkiatgumchai V, Kuan L, Gilman RC. Update on environmental risk factors for attention-deficit/hyperactivity disorder. *Curr Psychiatry Rep* 2011; **13**: 333-344. [CrossRef](#) | [PubMed](#)

[76](#) Carpenter DO, Nevin R. Environmental causes of violence. *Physiol Behav* 2010; **99**: 260-268. [CrossRef](#) | [PubMed](#)

[77](#) Miodovnik A, Engel SM, Zhu C, et al. Endocrine disruptors and childhood social impairment. *Neurotoxicology* 2011; **32**:261-267. [CrossRef](#) | [PubMed](#)

[78](#) Volk HE, Lurmann F, Penfold B, Hertz-Picciotto I, McConnell R. Traffic-related air pollution, particulate matter, and autism. *JAMA Psychiatry* 2013; **70**: 71-77. [PubMed](#)

[79](#) Bandeen-Roche K, Glass TA, Bolla KI, Todd AC, Schwartz BS. Cumulative lead dose and cognitive function in older adults. *Epidemiology* 2009; **20**: 831-839. [CrossRef](#) | [PubMed](#)

[80](#) Lock EA, Zhang J, Checkoway H. Solvents and Parkinson disease: a systematic review of toxicological and epidemiological evidence. *Toxicol Appl Pharmacol* 2013; **266**: 345-355. [CrossRef](#) | [PubMed](#)

[81](#) Landrigan PJ, Sonawane B, Butler RN, Trasande L, Callan R, Droller D. Early environmental origins of

neurodegenerative disease in later life. *Environ Health Perspect* 2005; **113**: 1230-1233. [CrossRef](#) | [PubMed](#)

[82](#) Lauterbach M, Solak E, Kaes J, Wiechelt J, Von Mach MA, Weilemann LS. Epidemiology of hydrogen phosphide exposures in humans reported to the poison center in Mainz, Germany, 1983–2003. *Clin Toxicol* 2005; **43**: 575-581. [PubMed](#)

[83](#) Demarest C, Torgovnick J, Sethi NK, Arsura E, Sethi PK. Acute reversible neurotoxicity associated with inhalation of ethyl chloride: a case report. *Clin Neurol Neurosurg* 2011; **113**: 909-910. [CrossRef](#) | [PubMed](#)

[84](#) Imamura T, Yanagawa Y, Nishikawa K, Matsumoto N, Sakamoto T. Two cases of acute poisoning with acetamiprid in humans. *Clin Toxicol* 2010; **48**: 851-853. [PubMed](#)

[85](#) Veale DJ, Wium CA, Muller GJ. Amitraz poisoning in South Africa: a two year survey (2008–2009). *Clin Toxicol* 2011; **49**:40-44. [PubMed](#)

[86](#) Sung YF, Huang CT, Fan CK, Lin CH, Lin SP. Avermectin intoxication with coma, myoclonus, and polyneuropathy. *Clin Toxicol* 2009; **47**: 686-688. [PubMed](#)

[87](#) Yang CC. Acute human toxicity of macrocyclic lactones. *Curr Pharm Biotechnol* 2012; **13**: 999-1003. [CrossRef](#) | [PubMed](#)

[88](#) Lee SJ, Mulay P, Diebolt-Brown B, et al. Acute illnesses associated with exposure to fipronil—surveillance data from 11 states in the United States, 2001–2007. *Clin Toxicol* 2010; **48**: 737-744. [PubMed](#)

[89](#) Malhotra RC, Ghia DK, Cordato DJ, Beran RG. Glyphosate-surfactant herbicide-induced reversible encephalopathy. *J Clin Neurosci* 2010; **17**: 1472-1473. [CrossRef](#) | [PubMed](#)

[90](#) David D, Prabhakar A, Peter JV, Pichamuthu K. Human poisoning with hexastar: a hexaconazole-containing agrochemical fungicide. *Clin Toxicol* 2008; **46**: 692-693. [PubMed](#)

[91](#) Shadnia S, Moghaddam HH. Fatal intoxication with imidacloprid insecticide. *Am J Emerg Med* 2008; **26**: 634.e1-634.e4. [CrossRef](#) | [PubMed](#)

[92](#) Deng X, Li G, Mei R, Sun S. Long term effects of tetramine poisoning: an observational study. *Clin Toxicol* 2012; **50**: 172-175. [PubMed](#)

[93](#) Khalil M, Abudiab M, Ahmed AE. Clinical evaluation of 1,3-butadiene neurotoxicity in humans. *Toxicol Ind Health* 2007; **23**:141-146. [CrossRef](#) | [PubMed](#)

[94](#) Bellinger DC. A strategy for comparing the contributions of environmental chemicals and other risk factors to neurodevelopment of children. *Environ Health Perspect* 2012; **120**: 501-507. [CrossRef](#) | [PubMed](#)

[95](#) Grandjean P, Pichery C, Bellanger M, Budtz-Jorgensen E. Calculation of mercury's effects on neurodevelopment. *Environ Health Perspect* 2012; **120**: A452. [CrossRef](#) | [PubMed](#)

[96](#) Bellanger M, Pichery C, Aerts D, et al. Economic benefits of methylmercury exposure control in Europe: monetary value of neurotoxicity prevention. *Environ Health* 2013; **12**: 3. [CrossRef](#) | [PubMed](#)

[97](#) Trasande L, Liu Y. Reducing the staggering costs of environmental disease in children, estimated at \$76.6 billion in 2008. *Health Aff* 2011; **30**: 863-870. [PubMed](#)

[98](#) Pichery C, Bellanger M, Zmirou-Navier D, Glorennec P, Hartemann P, Grandjean P. Childhood lead exposure in France: benefit estimation and partial cost-benefit analysis of lead hazard control. *Environ Health* 2011; 10: 44. [CrossRef](#) | [PubMed](#)

[99](#) Lynn R, Vanhanen T. IQ and the wealth of nations. Westport: Praeger, 2002.

[100](#) Blacksmith Institute. The world's worst pollution problems: assessing health risks at hazardous waste sites. New York: Blacksmith Institute, 2012.

[101](#) Trasande L, Massey RI, DiGangi J, Geiser K, Olanipekun AI, Gallagher L. How developing nations can protect children from hazardous chemical exposures while sustaining economic growth. *Health Aff* 2011; 30: 2400-2409. [PubMed](#)

[102](#) Nevin R. Understanding international crime trends: the legacy of preschool lead exposure. *Environ Res* 2007; 104: 315-336. [CrossRef](#) | [PubMed](#)

[103](#) Schwartz J. Societal benefits of reducing lead exposure. *Environ Res* 1994; 66: 105-124. [CrossRef](#) | [PubMed](#)

[104](#) National Research Council. Toxicity testing in the 21st century: a vision and a strategy. Washington, DC: National Academies Press, 2007.

[105](#) Makris SL, Raffaele K, Allen S, et al. A retrospective performance assessment of the developmental neurotoxicity study in support of OECD test guideline 426. *Environ Health Perspect* 2009; 117: 17-25. [CrossRef](#) | [PubMed](#)

[106](#) Rovida C, Longo F, Rabbit RR. How are reproductive toxicity and developmental toxicity addressed in REACH dossiers?. *Altex* 2011; 28: 273-294. [PubMed](#)

[107](#) Collins FS, Gray GM, Bucher JR. Toxicology. Transforming environmental health protection. *Science* 2008; 319: 906-907. [CrossRef](#) | [PubMed](#)

[108](#) Crofton KM, Mundy WR, Lein PJ, et al. Developmental neurotoxicity testing: recommendations for developing alternative methods for the screening and prioritization of chemicals. *Altex* 2011; 28: 9-15. [PubMed](#)

[109](#) Audouze K, Grandjean P. Application of computational systems biology to explore environmental toxicity hazards. *Environ Health Perspect* 2011; 119: 1754-1759. [PubMed](#)

[110](#) Willighagen EL, Jeliaskova N, Hardy B, Grafstrom RC, Spjuth O. Computational toxicology using the OpenTox application programming interface and Bioclipse. *BMC Res Notes* 2011; 4: 487. [PubMed](#)

[111](#) National Research Council. Science and decisions: advancing risk assessment. Washington, DC: National Academies Press, 2009.

[112](#) Late lessons from early warnings: science precaution, innovation.. Copenhagen: European Environment Agency, 2013.

[113](#) Moodie R, Stuckler D, Monteiro C, et al. Profits and pandemics: prevention of harmful effects of tobacco, alcohol, and ultra-processed food and drink industries. *Lancet* 2013; 381: 670-679. [Summary](#) | [Full Text](#) | [PDF\(232KB\)](#) | [CrossRef](#) | [PubMed](#)

[114](#) Grandjean P. Seven deadly sins of environmental epidemiology and the virtues of

precaution. *Epidemiology* 2008; 19:158-162. [CrossRef](#) | [PubMed](#)

115 Grandjean P, Eriksen ML, Ellegaard O, Wallin JA. The Matthew effect in environmental science publication: a bibliometric analysis of chemical substances in journal articles. *Environ Health* 2011; 10: 96. [PubMed](#)

methanol, half-life 3 hours in blood, enters every cell in adult and fetus, made into uncontrolled formaldehyde by ADH1 enzyme, causing random epigenetic methylation, and thus birth defects -- WC Monte paradigm: Rich Murray 2014.02.20

Prof. Woodrow C. Monte, Food Science and Nutrition, Arizona State University, retired 2004, gives a free online archive of 782 full text medical references at [WhileScienceSleeps.com](#) ...

Major methanol sources are cigarette and wood smoke, aspartame, and fruits juices and vegetables in cans and jars.

Methanol acts as a "Trojan horse" agent, releasing formaldehyde inside cells within 20 tissues in the adult and fetus -- random epigenetic modification is the major toxic process, initiating many chronic diseases and birth defects.

Only humans cells lack a functioning biochemical defense against the ADH1 enzyme, in high levels in 20 tissues, rapidly making methanol into uncontrolled, free floating highly reactive acidic hydrated formaldehyde right inside the cytosol. Thus, humans are ten to a hundred times more vulnerable than any other creature.

careful expert lifetime study on mice shows liver and lung cancers from aspartame, M Soffritti et al, Ramazzini Institute, Italy, checked by US National Toxicology Program experts, confirms many previous studies from 2001 on: Rich Murray 2011.02.27
<http://rmforall.blogspot.com/2011/02/careful-expert-lifetime-study-on-mice.html>
<http://health.groups.yahoo.com/group/aspartameNM/message/1619>

Prof. Erik Millstone 2013.12.16 crisp critique of EFSA blatant pro-industry bias on 2013.12.10 aspartame decision -- Sepp Hasslberger blog: Rich Murray 2014.01.07
<http://rmforall.blogspot.com/2014/01/prof-erik-millstone-20131216-crisp.html>

research on aspartame (methanol, formaldehyde, formic acid) toxicity: Rich Murray 2004.07.11 2014.01.21
<http://rmforall.blogspot.com/2014/01/research-on-aspartame-methanol.html>
<http://groups.yahoo.com/group/aspartameNM/message/1806> part 1 of 2
<http://groups.yahoo.com/group/aspartameNM/message/1809> part 2 of 2
<http://groups.yahoo.com/group/aspartameNM/message/1100> original

Methanol (wood alcohol) from cigarettes and aspartame circulates with blood half-life 3 hours, entering every cell -- made into uncontrolled formaldehyde inside cells with high ADH1 enzyme levels -- WC

Monte paradigm: Rich Murray 2014.02.04

similar macular harm in multiple sclerosis as from formaldehyde made by ADH enzyme inside retina capillary walls from methanol, Prof. Woodrow C. Monte text "While Science Sleeps" 2012 Jan -- some quotes re retina harm: Rich Murray 2012.05.10

<http://rmforall.blogspot.com/2012/05/similar-macular-harm-in-multiple.html>

Only humans cells lack a functioning biochemical defense against the ADH1 enzyme, in high levels in 20 tissues, rapidly making methanol into uncontrolled, free floating highly reactive acidic hydrated formaldehyde right inside the cytosol. Thus, humans are ten to a hundred times more vulnerable than any other creature.

Evidence exists that autism results from exposure to pregnant women in the fourth week, since ADH1 levels are high in the Purkinje cells of the vermis in the cerebellum, while other plausible birth defects include spina bifida, premature birth, and Fetal Alcohol Spectrum Disorder.

The leading methanol sources are cigarette smoke and aspartame (E951).

WC Monte gives 782 free full text medical research references at WhileScienceSleeps.com .

California OEHHA sets methanol ingestion level 23 mg daily, same as from 1 can aspartame diet soda, 10 cigarettes, 3 tomatoes, or 4 cans green beans: Rich Murray 2013.07.03

<http://rmforall.blogspot.com/2013/07/california-oe-ha-sets-methanol.html>

"However, the anticipated exposure to methanol from consumption of aspartame would not be considered an exposure within the meaning of Proposition 65 because aspartame is not listed under Proposition 65."

[Rich Murray: Many pregnant women drink one 12-oz can aspartame diet drink daily, with 200 mg aspartame that gives 11% methanol, 22 mg, which is just under the OEHHA limit of 23 mg daily.

The smoke from 10 cigarettes gives 20 mg methanol, the same as from 3 full size fresh tomatoes, or 4 cans of unfresh green beans.]

smoke from a pack cigarettes gives 40 mg methanol (wood alcohol), same as from 2 aspartame diet drinks -- becomes formaldehyde inside brain and retina cells via ADH1 enzyme -- WC Monte paradigm: Rich Murray 2013.08.30

11% of aspartame is methanol, which becomes free floating formaldehyde inside human cells -- methanol also in cigarettes and canned fruits and vegetables: Rich Murray 2013.08.30

Human epidemiological studies so far fail to control for additional common methanol sources: cigarettes and wood and peat smoke, smoked foods, fresh tomatoes, and degraded pectins from unfresh fruits juices vegetables preserved wet at room temperature in sealed cans jars plastic containers...

autism as a birth defect from epigenetic methylation by formaldehyde made from methanol by ADH1 enzyme inside Purkinje cells in vermis in cerebellum and in inner walls of brain blood vessels -- Prof. WC Monte paradigm: Rich Murray 2013.04.26

<http://rmforall.blogspot.com/2013/04/autism-as-birth-defect-from-epigenetic.html>

CA Pardo autism brain autopsy findings in 2005 fit WC Monte paradigm -- methanol with blood half-life 3 hours is made by ADH1 enzyme into free floating formaldehyde in 20 defenseless human cells in 20 tissues: Rich Murray 2013.07.21

<http://rmforall.blogspot.com/2013/07/ca-pardo-autism-brain-autopsy-findings.html>

The Woodrow C. Monte methanol/formaldehyde toxicity paradigm is that concentrations of ADH1 enzyme, well known to exist inside blood vessel wall cells in specific tissues, quickly turn methanol into formaldehyde inside the vessel cells, in humans only -- the highly reactive formaldehyde diffuses to penetrate adjacent tissue cells, binding to DNA, RNA, and proteins, attracting macrophages, which die, creating complex, expanding micro lesions, leading to many modern "diseases of civilization", Alzheimer's, arthritis, diabetes, multiple sclerosis, lupus -- as well as later cancers -- also serious birth defects in the fetal brain in the fourth week of pregnancy, spinal bifida and autism.

Aspartame is 11% methanol, 22 mg per can of diet drink -- similar levels of methanol come from wood and cigarette smoke, heated and canned fruits juices vegetables, fermented and smoked foods, some wines and liquors, vehicle fuels, many cleaners and solvents, chemical medical autopsy mortuary facilities, heated wood in particleboard and paper factories, and more.

WC Monte submits robust evidence for multiple sclerosis, which he concludes proves methanol to be the proximate toxic cause, since ADH1 enzyme is within the cells of the inner linings of brain blood vessels, the Purkinje cells of the vermis of the cerebellum, and rods and cones of the retina -- ADH1 quickly turns methanol into free floating formaldehyde within these cells, disrupting the blood brain barrier...

See also:

James McDonald to EFSA, outdated aspartame ADI gives methanol 35 times too high for human safety, ten minute talk at April 9 public sharing, Brussels: Rich Murray 2013.04.15

<http://rmforall.blogspot.com/2013/04/james-mcdonald-to-efsa-outdated.html>

aspartame harm in rat brain from 75 mg/kg gives human ADI 0.75 mg/kg, 53 times less than EU ADI 40 mg/kg, Ashok Iyyaswamy, SheelaDevi Rathinasamy, U. Madras 2012.08.03 free full text -- main methanol toxin is formaldehyde, not formate: Rich Murray 2013.06.01

<http://rmforall.blogspot.com/2013/06/aspartame-harm-in-rat-brain-from-75.html>

more lower aspartame and methanol ADIs from studies by RH Nair, SheelaDevi Rathinasamy, WC Monte, PS Jeganathan, A Namasivayam, Hazleton Labs, Searle Labs: Rich Murray 2013.06.01

<http://rmforall.blogspot.com/2013/06/more-lower-aspartame-and-methanol-adis.html>

Kate S. Collison et al show prediabetic harm in gene expression in mice fed lifetime aspartame, MSG, trans fats -- reduce human aspartame ADI 1000 times: Rich Murray 2013.07.30

<http://rmforall.blogspot.com/2013/07/kate-s-collison-et-al-show-prediabetic.html>

aspartame impairment of spatial cognition and insulin sensitivity in mice, focus on phenylalanine and aspartate [methanol also crosses placenta into fetus, turning into teratogenic formaldehyde], Kate S. Collison et al, PLoS One 2012.04.03: Rich Murray 2012.04.29

<http://rmforall.blogspot.com/2012/04/aspartame-impairment-of-spatial.html>

usual doses of aspartame proven to cause cancers, Michael F. Jacobson PhD, Director, Center for Science in the Public Interest -- also long 1985 statement: Rich Murray 2013.08.15

<http://rmforall.blogspot.com/2013/08/usual-doses-of-aspartame-proven-to.html>

highly competent, pithy analysis of aspartame cancer study by Eva S. Schernhammer at Harvard, William R. Ware, PhD, showing relevance of Woodrow C. Monte methanol-formaldehyde toxicity paradigm: Rich Murray 2012.12.03

<http://rmforall.blogspot.com/2012/12/highly-competent-pithy-analysis-of.html>

careful expert lifetime study on mice shows liver and lung cancers from aspartame, M Soffritti et al, Ramazzini Institute, Italy, checked by US National Toxicology Program experts, confirms many previous studies from 2001 on: Rich Murray 2011.02.27

<http://rmforall.blogspot.com/2011/02/careful-expert-lifetime-study-on-mice.html>

The public EFSA session on aspartame safety on April 9 for 5 hours included an audience of about 50 experts and 10-20 ESFA staff in Brussels.

The release of the final EFSA review on aspartame safety will be delayed from April 15 to early December, 2013.

Extremely cogent multiple lines of robust evidence were briefly described that strongly support the methanol formaldehyde toxicity paradigm of Prof. Woodrow C. Monte, Prof. Food Science and Nutrition, Arizona State University, retired 2004 -- supported by an online archive of 782 free full text medical research references at www.WhileScienceSleeps.com.

It is clear that methanol is far more dangerous for chronic low level exposures than realized since 1890.

Major sources include the smoke from a pack of cigarettes, 40 mg methanol, the same as from 2 cans aspartame diet drink. It now seems likely that most cigarette diseases are actually methanol toxicity...

Methanol stays in the blood with a half-life of 3 hours, reaching every part of the body and the fetus with the bloodstream, and readily entering all cells.

Humans are uniquely vulnerable to methanol formaldehyde toxicity, as they lack a functioning catalase enzyme system, that in all other creatures serves to protect each cell against the rapid conversion of methanol into free floating formaldehyde right inside the cells of 20 specific tissues that have high levels of ADH1 enzyme.

The effects are used to good advantage in embalming and disinfection, as formaldehyde immediately bonds to and impairs DNA, RNA, and proteins, permanently disrupting cell biochemistry, cell by cell, as long as methanol is ingested -- leading to 20 specific chronic modern novel "diseases of civilization", that progress slowly and erratically, according to the ingestion of methanol from a variety of modern sources:

smoke from cigarettes, wood, and peat;

since 1983, aspartame, including from most chewing gums;

fresh tomatoes and black currants;

unfresh fruits juices vegetables cut up and preserved wet at room temperature in sealed cans jars plastic containers;

jams jellies marmalades;

smoked fermented spoiled foods;

many dark wines and liquors;

work at paper and wood factories, mortuaries, medical and chemical facilities;

Research since 2012 specifically shows the presence of formaldehyde bonded to cellular macromolecules inside cells after methanol ingestion -- the paradigm will be confirmed in detail very quickly, as science exponentially explores this simple breakthrough.

This presents the world food industry with an unprecedented opportunity to serve the huge public good by collaborating vigorously to eliminate all methanol exposures from foods and beverages. The Net guarantees that the news and evidence will spread explosively everywhere.

Paul Thomas MD Pediatrics and Integrative Medicine, Portland OR, praises "While Science Sleeps" at Amazon.com -- WC Monte paradigm of methanol formaldehyde toxicity via ADH1 enzyme in 20 human tissues, including fetus: Rich Murray 2013.04.03

<http://rmforall.blogspot.com/2013/04/paul-thomas-md-pediatrics-integrative.html>

Prof. Resia Pretorius letter re aspartame to EJCNC cites Prof. Woodrow C. Monte "While Science Sleeps" text, re methanol/formaldehyde toxicity paradigm: Rich Murray 2012.05.21

<http://rmforall.blogspot.com/2012/05/prof-resia-pretorius-letter-re.html>

Aspartame: The hidden danger [methanol/formaldehyde] in our midst and how it kills us, 12 page review of While Science Sleeps text (Woodrow C Monte), International Health News, whole June issue, Editor: William R Ware PhD: Rich Murray 2012.06.08

<http://rmforall.blogspot.com/2012/06/aspartame-hidden-danger.html>

Table 5.2 is the key chart -- ADH1 enzyme at high levels in 20 tissues in body and fetus makes methanol into formaldehyde right inside cells, initiating over 20 human diseases, with full text references, WC Monte paradigm: Rich Murray 2013.03.21

<http://rmforall.blogspot.com/2013/03/table-52-is-key-chart-adh1-enzyme-at.html>

"As a matter of course, every soul citizen of Earth has a priority to quickly find and positively share evidence for healthy and safe food, drink, environment, and society."

within the fellowship of service,

Rich Murray
MA Boston University Graduate School 1967 psychology
BS MIT 1964 history and physics

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